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**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Application Number: 10/539,726

Filing Date: July 19, 2006

Appellant(s): AMONTOV ET AL.

Michael J. Cooper
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed on July 19, 2010 appealing from the Office action mailed January 21, 2010.

(1) Real Party in Interest

The examiner has no comment on the statement, or lack of statement, identifying by name the real party in interest in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The following is a list of claims that are rejected and pending in the application:

Claims 1, 4-14, 17, and 20-23 are currently pending. Claims 1, 4-14, 17, and 20-22 are rejected. Claim 23 is withdrawn as being drawn to a non-elected invention.

(4) Status of Amendments After Final

The examiner has no comment on the appellant's statement of the status of amendments after final rejection contained in the brief.

(5) Summary of Claimed Subject Matter

The examiner has no comment on the summary of claimed subject matter contained in the brief.

(6) Grounds of Rejection to be Reviewed on Appeal

The examiner has no comment on the appellant's statement of the grounds of rejection to be reviewed on appeal. Every ground of rejection set forth in the Office action from which the appeal is taken (as modified by any advisory actions) is being maintained by the examiner except for the grounds of rejection (if any) listed under the subheading "WITHDRAWN REJECTIONS." New grounds of rejection (if any) are provided under the subheading "NEW GROUNDS OF REJECTION."

(7) Claims Appendix

The examiner has no comment on the copy of the appealed claims contained in the Appendix to the appellant's brief.

(8) Evidence Relied Upon

6,432,360	CHURCH	8-2002
2003/0044781 A1	KORLACH et al.	3-2003
5,686,271	MIAN et al.	11-1997

Richter, J., et al. "Nanoscale Palladium Metallization of DNA" Advanced Materials, Vol. 12, No. 7 (2000), pp. 507-510.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4-7, 9, 10, 14, 17, and 20-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Church (US 6,432,360 B1).

These claims are drawn to a method for producing a homogeneous monolayer of molecules on a surface comprising transferring seed molecules from a stamp to the surface and producing the homogeneous monolayer via amplification on the surface.

Regarding claim 1, Church teaches a method for producing a monolayer of molecules on a surface (see columns 8-15) comprising:

(a) loading a stamp with seed molecules (column 15, lines 1-55)
(b) transferring seed molecules from the stamp to a flat surface, where the transferring comprises transferring a fraction of the seed molecules loaded on the stamp to the flat surface and adsorbing the seed molecules to the surface (column 15, lines 52-55)
(c) self-completing amplification of the seed molecules via an amplifying reaction to produce the a homogeneous area comprising a monolayer of nucleic acids on the flat surface (column 15, line 56 teaches amplification of the transferred seed molecules; see column 13, line 58 – column 14, line 67 for further description of the amplification step).

Further regarding claim 1, since not all of the seed molecules are transferred during the microcontact printing step (see column 15), the adsorption of the seed molecules to the stamp is inherently stronger than the adsorption of the seed molecules to the surface.

Further regarding claim 1, Church also teaches an embodiment of the method that produces a monolayer wherein all of the nucleic acids comprising the monolayer are the same length (see column 21, lines 34-57). Also, it is noted that the monolayers resulting from the amplification reactions of Church consist of one type of molecule (nucleic acid or protein). Thus, Church teaches homogeneous monolayers as required by claim 1. Church further teaches that the monolayer produced via the disclosed method does not comprise diffusive seed molecules that can relocate and destroy amplification accuracy (column 15, lines 24-36; see also, column 7, lines 3-21, for example, where Church teaches that the transferred seed molecules are covalently attached to the surface, thereby precluding relocation of the transferred seed molecules via diffusion).

Regarding claim 4, Church teaches that the amplification comprises linear amplification of the seed molecules (see column 14, for example, where reverse transcription is a type of linear amplification).

Regarding claims 5 and 14, Church teaches PCR amplification of the seed molecules (see column 13, lines 60-65 and column 14, lines 8-12, for example), which is an exponential amplification method.

Regarding claims 6, 7, 9, and 10, the PCR amplification taught by Church is a directional amplification method that is inherently controlled by the geometry of the seed molecules. The amplification is also controlled by application of an external force, specifically heating (see, for

example, columns 13-14). Finally, the nucleic acids amplified by the method of Church are inherently conductive structures.

Regarding claim 17, Church teaches *in vitro* translation to generate a protein monolayer (column 9, lines 10-15).

Regarding claim 20, the monolayer produced by Church inherently protects the surface from etchants.

Regarding claim 21, Church teaches that the monolayer comprises DNA (see, for example, column 15, lines 37-56).

Regarding claim 22, Church teaches repeating the transferring and amplifying steps on a plurality of surfaces before reloading the stamp with seed molecules (see, for example, column 3, lines 58-63).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Church (US 6,432,360 B1) in view of Richter et al. (Advanced Materials (2000) 12(7): 507-510).

Claim 8 is drawn to the method of claim 6, further comprising electroless plating of the directionally amplified seed molecules with a metal.

Church teaches the method of claims 1, 4-7, 9, 10, 14, 17, and 20-22, as discussed above.

Church does not teach electroless plating of the directionally amplified seed molecules with a metal.

Richter teaches that DNA molecules can be metallized and electrolessly plated to form useful nanostructures such as nanowires (see pages 508-510).

It would have been *prima facie* obvious for one of ordinary skill in the art at the time of invention to apply the teachings of Richter to the methods taught by Church. An ordinary artisan would have been motivated to metallize and electrolessly plate the amplified nucleic acids on the replica plate of Church as taught by Richter in order to obtain the ability to generate useful nanostructures, such as nanowires. Thus, the method of claim 8 is *prima facie* obvious over Church in view of Richter.

Claims 11 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Church (US 6,432,360 B1) in view of Korlach et al. (US 2003/0044781 A1).

Claims 11 and 13 are drawn to the method of claim 10, wherein the directional amplification of the seed molecules is controlled via application of an electric force or a hydrodynamic force, respectively.

Church teaches the method of claims 1, 4-7, 9, 10, 14, 17, and 20-22, as discussed above.

Church does not teach controlling the amplification reaction with an electrical or hydrodynamic force.

Korlach teaches a method for producing a monolayer of molecules on a surface, comprising: (a) loading a stamp with seed molecules, (b) transferring the seed molecules from the stamp to the surface, and (c) directionally amplifying the seed molecules to produce the monolayer (see Figure 1 and paragraph 39).

Regarding claims 11 and 13, Korlach teaches that the directional amplification is controlled by application of an external force, specifically an electrical or hydrodynamic force (see paragraph 60, where the nucleotide substrates used in the amplification process are supplied by electrical or hydrodynamic forces).

It would have been *prima facie* obvious for one of ordinary skill in the art at the time of invention to control the directional amplification step in the methods taught by Church by applying any force known to be useful for controlling amplification, such as the electric and hydrodynamic forces taught by Korlach. An ordinary artisan would have recognized that these forces were art-recognized equivalents useful for achieving the same purpose, namely controlling directional amplification, and therefore, would have been motivated to substitute one for the other with a reasonable expectation of success. Also, see MPEP 2144.06, which states that the substitution of art-recognized equivalents known to be useful for the same purpose is *prima facie*

obvious. Thus, the methods of claims 11 and 13 are *prima facie* obvious over Church in view of Korlach in the absence of secondary considerations.

Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Church (US 6,432,360 B1) in view of Mian et al. (US 5,686,271).

Claim 12 is drawn to the method of claim 10, wherein the directional amplification reaction is controlled via application of a magnetic force.

Church teaches the method of claims 1, 4-7, 9, 10, 14, 17, and 20-22, as discussed above.

Church does not teach that the amplification is controlled by an applied magnetic force.

Mian teaches a method for conducting PCR using magnetic fields termed a “magnetic cycle reaction” or MCR. The MCR method taught by Mian comprises assembling a PCR reaction mixture, conducting multiple cycles of denaturation, annealing, and extension using an electromagnetic field to effect strand separation (see Example 7, column 16, line 50 – column 18, line 9). In the method of Mian, one primer is immobilized on a surface and the other primer is supplied in solution (see Example 7, column 16, lines 50-66, where one primer is immobilized on the bottom of a well of a microtiter plate and the other primer is added in solution).

Regarding claim 12, the PCR amplification taught by Mian is controlled by application of a magnetic field (see Example 7, column 16, line 50 – column 18, line 9).

Mian teaches that magnetic control of PCR amplification has a number of advantages relative to conventional PCR, where high temperatures are used to denature double-stranded DNA targets. Specifically, Mian teaches that the use of electromagnetism for strand separation eliminates the need to use a thermophilic polymerase in the PCR reaction and permits the use of

mesophilic polymerases. Mian teaches that this is advantageous, because mesophilic polymerases have higher fidelity, faster extension rates, and greater processivity than their thermophilic counterparts, thus resulting in a faster, more accurate amplification process that is capable of amplifying longer targets (column 2, lines 19-45).

It would have been *prima facie* obvious for one of ordinary skill in the art at the time of invention to substitute the MCR reaction as taught by Mian for the conventional nucleic acid amplification reactions taught by Church. An ordinary artisan would have been motivated to do so, since Mian taught that electromagnetic denaturation permitted the use of mesophilic polymerases with higher fidelity, faster extension rates and greater processivity than their thermophilic counterparts, thus resulting in a faster, more accurate amplification process capable of amplifying longer templates (column 2, lines 19-45). Thus, the method of claim 12 is *prima facie* obvious over Church in view of Mian.

(10) Response to Argument

Rejection #1 – Rejection of claims 1, 4-7, 9, 10, 14, 17, and 20-22 under 35 U.S.C.

102(b) as being anticipated by Church

Appellant presents arguments with respect to independent claim 1 and also with respect to dependent claims 4, 17, and 20-22.

Argument #1 – Church does not teach all of the elements of independent claim 1

Appellant argues that Church does not teach "self-completing amplification of the seed molecules via an amplifying reaction to produce a monolayer on the flat surface, wherein self-completing amplification of the seed molecules via an amplifying reaction to produce the

monolayer comprises producing a homogeneous area that comprises a monolayer of molecules on the flat surface and has no diffusive seed molecules that can relocate and destroy amplification accuracy" (pages 5-6). Appellant argues that Church teaches randomly patterned arrays of nucleic acid molecules, and, therefore, does not meet the requirement in claim 1 for production of a homogeneous area comprising a monolayer of molecules (pages 5-6). Appellant also argues that Church teaches the use of swollen gels as the soft transfer medium, and that these materials are not capable of being used to effect the self-completing amplification reaction recited in claim 1 (page 6). Finally, Appellant argues that Church does not meet the requirement in claim 1 for the monolayer to have no diffusive seed molecule component that can relocate and destroy amplification accuracy (page 7).

Appellant's arguments regarding the teachings of Church with respect to independent claim 1 were not persuasive, because the replica transfer and amplification steps taught by Church at columns 8-15 result in a self-completing amplification reaction that produces a homogeneous area comprising a monolayer of nucleic acid molecules having the same length attached to a flat surface. As noted by Appellant at pages 5-6, the arrays produced by the method of Church are randomly patterned, but Church teaches that the arrays are "randomly patterned" with respect to the identity of the molecules at each discrete location and further teaches that the array surface is patterned such that different molecules are present in different features (see, for example, column 1, line 64 – column 2, line 19). Thus, the production of a randomly patterned array does not preclude the formation of a homogeneous area comprising a monolayer on the flat surface as Appellant's arguments suggest.

It is also noted that the methods of Church are not limited to gels as argued by Appellant. Rather, gels are only an exemplary embodiment of Church, who also teaches flat surfaces that support self-completing amplification reactions (see, *e.g.*, column 4, lines 25-30, where Church teaches the use of nylon or cellulose surfaces). It is further noted that, although Church teaches that preferred supports used to practice the method are semi-solid and include gels, such as polyacrylamide gels, the reference is clearly not limited to these embodiments as Appellant argues at page 10 (see, for example, column 3, lines 18-20, column 9, line 24 - column 10, line 22, and column 11, lines 19-37). As noted in MPEP 2123, the prior art is relevant for all that it contains or suggests to the ordinary artisan, including non-preferred embodiments.

Finally, Appellant's arguments regarding the teachings of Church with respect to the requirement for the monolayer to contain no diffusive seed molecules that can relocate and destroy amplification accuracy were unpersuasive, because the discussion of Church at column 9 clearly indicates that, although a limited amount of diffusion can occur, it does **not** occur to an extent that amplification accuracy is destroyed. Appellant's arguments at page 7 concerning the teachings of Church with respect to tolerance of mismatches at the priming site were also unpersuasive, because tolerance of mismatches is only an optional feature of the methods of Church. As noted in MPEP 2123, the prior art is relevant for all that it contains or suggests to the ordinary artisan, including non-preferred embodiments. Furthermore, it is noted that the term "destroy amplification accuracy" is a broad term that can be reasonably interpreted to encompass amplification reactions conducted at 100% accuracy or a slightly lower degree of accuracy, such as the accuracy levels attained when the embodiments of Church including a limited degree of

mismatch tolerance taught by Church in column 11 are included, so long as substantially accurate amplification is achieved.

Argument #2 – Church does not teach all of the elements of dependent claim 4

Appellant argues that Church does not meet all of the requirements of dependent claim 4, because the reference only teaches reverse transcription as a means to create reverse transcripts that are then subjected to an amplification process (page 8). This argument was not persuasive, because Church teaches at column 14 that the solid-phase *in situ* amplification step (i.e., the self-completing amplification reaction) may be conducted by self-sustained sequence replication (3SR) or NASBA, which each comprise linear amplification of the seed molecules, specifically during the initial reverse transcription step of the process (column 14). It is noted that claim 4 does not require the amplifying reaction to be completely linear. Claim 4 only requires that the amplification process comprises linear amplification of the seed molecule, which occurs during the reverse transcription step of the 3SR and NASBA methods taught by Church.

Argument #3 – Church does not teach all of the elements of claims 17 and 20-22

Appellant first argues that Church does not teach all of the elements of claim 1, and, therefore, cannot be considered to teach all of the elements of dependent claims 17 and 20-22 (page 9). This argument was not persuasive, because, as discussed above, Church teaches all of the elements of independent claim 1 as well as claims 17 and 20-22.

Appellant also argues that Church does not teach all of the elements of claim 22, because the reference does not teach repeating the original transfer and amplification steps before

reloading the stamp with seed molecules as required by the claim (page 9). This argument was not persuasive, because Church clearly teaches at column 3, lines 45-63 that the method comprises repeating the transfer and amplification steps such that multiple solid support surfaces possess the required monolayer of nucleic acids. It is noted that claim 22 does not require the prior art to positively recite a step of reloading the stamp after the step of repeating the transfer and amplification steps as Appellant argues at page 9. Claim 22 only requires that multiple steps of transfer and amplification occur in the absence of (*i.e.*, before) reloading of the stamp. Since Church teaches conducting the required plurality of transfer and amplification steps and does not teach that a reloading step is conducted before each transfer step (see column 3), Church meets the requirements of claim 22.

For these reasons, Appellant's arguments filed on July 19, 2010 were not persuasive, and claims 1, 4-7, 9, 10, 14, 17, and 20-22 are considered to be anticipated by Church.

Rejection #2 - Rejection of claim 8 under 35 U.S.C. 103(a) as being unpatentable over Church in view of Richter

Appellant first argues that Church does not teach all of the elements of independent claim 1, from which claim 8 depends, and that the teachings of Richter do not remedy this deficiency in the primary reference (see pages 9-10). This argument was not persuasive, because, as discussed above, Church teaches all of the elements of independent claim 1.

Appellant also argues that there is no motivation to combine the teachings of Church and Richter, because DNA that is replicated in a gel as taught by Church cannot be metallized by the method disclosed in Richter (page 10). In response to this argument that there is no teaching,

suggestion, or motivation to combine the references, the examiner recognizes that obviousness may be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988), *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992), and *KSR International Co. v. Teleflex, Inc.*, 550 U.S. 398, 82 USPQ2d 1385 (2007). In this case, the ordinary artisan would have been motivated to metallize and electrolessly plate the amplified nucleic acids on the replica plate of Church as taught by Richter in order to obtain the ability to generate useful nanostructures, such as nanowires. It is also noted that the methods of Church are not limited to gels as argued by Appellant at page 10. Rather, gels are only an exemplary embodiment of Church, who also teaches flat surfaces upon which metallization can occur (see, e.g., column 4, lines 25-30, where Church teaches the use of nylon or cellulose surfaces). It is further noted that, although Church teaches that preferred supports used to practice the method are semi-solid and include gels, such as polyacrylamide gels, the reference is clearly not limited to these embodiments as Appellant argues at page 10 (see, for example, column 3, lines 18-20, column 9, line 24 - column 10, line 22, and column 11, lines 19-37). As noted in MPEP 2123, the prior art is relevant for all that it contains or suggests to the ordinary artisan, including non-preferred embodiments.

For these reasons, Appellant's arguments filed on July 19, 2010 were not persuasive, and claim 8 is considered to be obvious in view of the combined teachings of Church and Richter.

**Rejection #3 – Rejection of claims 11 and 13 under 35 U.S.C. 103(a) as being
unpatentable over Church in view of Korlach**

Appellant first argues that Church does not teach all of the elements of independent claim 1, from which claims 11 and 13 depend, and that the teachings of Korlach do not remedy this deficiency in the primary reference (see page 11). This argument was not persuasive, because, as discussed above, Church teaches all of the elements of independent claim 1.

Appellant also argues that there is no motivation to combine the teachings of Church and Korlach, specifically because Korlach teaches away from the proposed combination by teaching away from an amplification step (page 11). Appellant's arguments regarding teaching away in Korlach were unpersuasive, because the reference is not relied upon to suggest the inclusion of an amplification step as Appellant appears to argue at page 11, but, rather, to establish that the claimed electrical and hydrodynamic methods for controlling directional amplification were known in the art at the time of invention, and, therefore, were obvious choices for controlling the directional amplification reaction of Church.

Appellant further argues that Korlach does not, in fact, teach controlling amplification via hydrodynamic or electrical force as required by claims 11 and 13 (pages 11-12). This argument was not persuasive, because the claims are not as narrow as Appellant's argues. The claims as written encompass controlling amplification by using electrical force or hydrodynamic force to control the movement of nucleotides during the reaction as described by Korlach. As noted in MPEP 2111, the claims are to be given their broadest reasonable interpretation that is consistent with the specification. In this case, the specification does not set forth an explicit and limiting definition for "controlling a directional amplification reaction using an electrical or

hydrodynamic force", and the electrical and hydrodynamic control taught by Korlach is not inconsistent with the specification. It is also noted that, although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

For these reasons, Appellant's arguments filed on July 19, 2010 were not persuasive, and claims 11 and 13 are considered to be obvious in view of the combined teachings of Church and Korlach.

Rejection #4 – Rejection of claim 12 under 35 U.S.C. 103(a) as being unpatentable over Church in view of Mian

Appellant argues that Church does not teach all of the elements of independent claim 1, from which claim 12 depends, and that the teachings of Mian do not remedy this deficiency in the primary reference (see page 12). This argument was not persuasive, because, as discussed above, Church teaches all of the elements of independent claim 1. For these reasons, Appellant's arguments filed on July 19, 2010 were not persuasive, and claim 12 is considered to be obvious in view of the combined teachings of Church and Mian.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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